

has identity with the *ced-3* and Interleukin-1 $\beta$  convertase (ICE) genes, said isolated protein having an alteration in the amino acid sequence of the product of a gene which has identity with the *ced-3* and ICE genes, said alteration corresponding to an amino acid substitution in the sequence of SEQ ID NO: 4 or 30 selected from the group consisting of:

- i) F at amino acid 26;
- ii) R at amino acid 65;
- iv) S at amino acid 287;
- v) truncation of said protein after amino acid 323;
- vi) truncation of said protein after amino acid 339;
- vii) V at amino acid 361;
- viii) K at amino acid 390; and
- ix) F at amino acid 393.

2. (Amended) The protein of claim 1, which is a protease cleaving after aspartate residues.

3. (Amended) The protein of claim 1, which is a cysteine protease.

4. (Amended) An isolated ICE polypeptide (SEQ ID NO: 4 or 30) having an alteration which reduces the proteolytic activity of the protein, wherein said alteration is an amino acid substitution selected from the group consisting of:

- a) F at amino acid 26;
- b) R at amino acid 65;
- c) S at amino acid 287;
- d) truncation of said polypeptide after amino acid 323;
- e) truncation of said polypeptide after amino acid 339;
- f) V at amino acid 361;

- g) K at amino acid 390; and
- h) F at amino acid 393.

6. (Amended) A constitutively activated cell death protein comprising an amino acid sequence having deletions of the inhibitory amino-terminal portions, said sequence comprising a portion of the Ced-3 protein shown in SEQ ID NO: 2 of Figure 6A or SEQ ID NO: 29, said portion selected from the group consisting of:

- a) the amino acids from 150 to 503 (SEQ ID NO: 20);
- b) the amino acids from 373 to 503 (SEQ ID NO: 21); and
- c) the amino acids from 150 to 372 (SEQ ID NO: 22).

7. (Amended) The protein of claim 6, further comprising a subportion of the region of Ced-3 from amino acids 1 to 149, as shown in SEQ ID NO: 2 of Figure 6A or SEQ ID NO: 29, said subportion enhancing the proteolytic activity of the protein.

8. (Amended) A constitutively activated cell death protein comprising an amino acid sequence having deletions of the inhibitory amino-terminal portions, said protein

- (a) having a substitution in the amino acid sequence ICE relative to the ICE sequence shown in Figure 6A (SEQ ID NO: 4) or SEQ ID NO: 30; and
- (b) comprising a portion of the ICE sequence in SEQ ID NO: 4 or 30, said portion selected from the group consisting of:

- i) the amino acids from 111 to 404 (SEQ ID NO: 23);
- ii) the amino acids from 298 to 404 (SEQ ID NO: 24); and
- iii) the amino acids from 111 to 297 (SEQ ID NO: 25).

9. (Amended) An isolated protein having an amino acid alteration in the NEDD-2 protein (SEQ ID NO: 28), said alteration being an alteration which inactivates said protein, wherein said alteration is an amino acid substitution of A to V at amino acid

397, relative to the sequence of SEQ ID NO: 28.

10. (Amended) An isolated protein having an amino acid alteration in the NEDD-2 protein (SEQ ID NO: 28, said alteration being an alteration which inactivates said protein, wherein said alteration is an amino acid substitution of C to A at amino acid 319, relative to the sequence of SEQ ID NO: 28.

11. (Amended) An isolated protein having an amino acid alteration in the NEDD-2 protein (SEQ ID NO: 28), said alteration being an alteration which inactivates said protein, wherein said alteration is an amino acid substitution of C to S at amino acid 319, relative to the sequence of SEQ ID NO: 28.

12. (Amended) An isolated protein which is selected from the group consisting of Ced-3 (SEQ ID NO: 2 or 29), ICE (SEQ ID NO: 4 or 30), and NEDD-2 (SEQ ID NO: 28), said protein having an alteration selected from the group consisting of a substitution in amino acid:

- a) Ser 183 of Ced-3 or Ser 126 of ICE;
- b) Met 234 of Ced-3;
- c) Arg 242 of Ced-3;
- d) Leu 246 of Ced-3 or Leu 166 of ICE;
- e) Ile 247 of Ced-3 or Ile 167 of ICE;
- f) Ile 248 of Ced-3 or Ile 168 of ICE;
- g) Asn 250 of Ced-3 or Asn 170 of ICE;
- h) Phe 253 of Ced-3 or Phe 173 of ICE;
- i) Arg 259 of Ced-3 or Arg 179 of ICE;
- j) Gly 261 of Ced-3 or Gly 181 of ICE;
- k) Asp 265 of Ced-3 or Asp 185 of ICE;
- l) Gly 277 of Ced-3 or Gly 197 of ICE;

- m) Tyr 278 of Ced-3 or Tyr 198 of ICE;
- n) Val 280 of Ced-3 or Val 200 of ICE;
- o) Lys 283 of Ced-3 or Lys 203 of ICE;
- p) Asn 285 of Ced-3 or Asn 205 of ICE;
- q) Leu 286 of Ced-3 or Leu 206 of ICE;
- r) Thr 287 of Ced-3 or Thr 207 of ICE;
- s) Met 291 of Ced-3 or Met 211 of ICE;
- t) Phe 298 of Ced-3 or Phe 218 of ICE;
- u) His 304 of Ced-3 or His 244 of ICE;
- v) Asp 306 of Ced-3 or Asp 228 of ICE;
- w) Ser 307 of Ced-3 or Ser 229 of ICE;
- x) Leu 310 of Ced-3 or Leu 232 of ICE;
- y) Val 311 of Ced-3 or Val 233 of ICE;
- z) Ser 314 of Ced-3 or Ser 236 of ICE;
- aa) His 315 of Ced-3 or His 237 of ICE;
- bb) Gly 316 of Ced-3 or Gly 238 of ICE;
- cc) Ile 321 of Ced-3 or Ile 243 of ICE;
- dd) Gly 323 of Ced-3 or Gly 245 of ICE;
- ee) Ile 334 of Ced-3 or Ile 261 of ICE;
- ff) Asn 339 of Ced-3 or Asn 226 of ICE;
- gg) Pro 344 of Ced-3 or Pro 271 of ICE;
- hh) Leu 346 of Ced-3 or Leu 273 of ICE;
- ii) Lys 349 of Ced-3 or Lys 276 of ICE;
- jj) Pro 350 of Ced-3 or Pro 277 of ICE;
- kk) Lys 351 of Ced-3 or Lys 278 of ICE;
- ll) Gln 356 of Ced-3, Gln 283 of ICE, or Glu 323 of NEDD-2;
- mm) Ala 357 of Ced-3, Ala 284 of ICE, or Thr 324 of NEDD-2;
- nn) Cys 358 of Ced-3 or Cys 285 of ICE;

- oo) Arg 359 of Ced-3, Arg 286 of ICE, or Arg 326 of NEDD-2;
- pp) Gly 360 of Ced-3, Gly 287 of ICE, or Gly 327 of NEDD-2;
- qq) Asp 371 of Ced-3 or Asp 297 of ICE;
- rr) Asp 414 of Ced-3, Asp 326 of ICE, or Asp 362 of NEDD-2;
- ss) Arg 429 of Ced-3, Arg 341 of ICE, or Arg 377 of NEDD-2;
- tt) Gly 434 of Ced-3, Gly 346 of ICE, or Gly 382 of NEDD-2;
- uu) Ser 435 of Ced-3, Ser 347 of ICE, or Ser 383 of NEDD-2;
- vv) Ile 438 of Ced-3, Ile 350 of ICE, Ile 386 of NEDD-2;
- ww) Ala 449 of Ced-3, Ala 361 of ICE, or Ala 388 of NEDD-2;
- xx) Val 454 of Ced-3, Val 366 of ICE, or Val 402 of NEDD-2;
- yy) Leu 488 of Ced-3, Leu 394 of ICE, or Leu 438 of NEDD-2;
- zz) Tyr 493 of Ced-3, Tyr 399 of ICE, or Tyr 443 of NEDD-2; and
- aaa) Pro 496 of Ced-3, Pro 402 of ICE, or Pro 446 of NEDD-2.

13. (Amended) An isolated protein selected from the group consisting of Ced-3 (SEQ ID NO: 2 or 29), NEDD-2 protein (SEQ ID NO: 28), and ICE (SEQ ID NO: 4 or 30), said protein having an amino acid alteration, wherein said alteration is at Cys 358 of Ced-3, Cys 319 of NEDD-2, or Cys 285 of ICE.

14. (Amended) The isolated protein of claim 13, wherein said amino acid alteration at Cys 358 of Ced-3 or Cys 285 of ICE is a Cys to Ala alteration.

15. (Amended) The isolated protein of claim 13, wherein said protein is ICE and said amino acid alteration is at conserved amino acid Cys 285 of said ICE.

16. (Amended) The isolated protein of claim 13, wherein said protein is NEDD-2 and said alteration is at conserved amino acid amino acid 319 of said NEDD-2 (SEQ ID NO: 28).